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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Noel et al.

Title: METHODS AND COMPOSITIONS FOR DETERMINING ENZYMATIC ACTIVITY

Appl. No.: 10/031,918

Filing Date: 09/24/2002

Examiner: Nashed, Nashaat T.

Art Unit: 1656

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CERTIFICATE OF FACSIMILE TRANSMISSION
I hereby certify that this paper is being facsimile transmitted to the United States Patent and Trademark Office, Alexandria, Virginia on the date below.

Stephen E. Reiter
(Printed Name)

(Signature)

September 29, 2006
(Date of Deposit)

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Joseph P. Noel, being duly warned, hereby declare and say that:

1. I, Joseph P. Noel, am a citizen of the United States, residing in San Diego, CA. I am currently employed by the Howard Hughes Medical Institute and work at the Salk Institute for Biological Studies, La Jolla, CA, as Professor in The Jack H. Skirball Center for Chemical Biology and Proteomics.

2. I am an inventor of the above-referenced invention and have read the specification and claims thereof.

3. I have read the Office Action dated May 31, 2006, for the above-referenced application.

4. The Office Action repeatedly mischaracterizes the teachings of the above-referenced application by asserting that crystallization conditions for chalcone synthase and specific mutants are not fully described in the specification. Examples of such mischaracterizations include the following passages from the Office Action:

- "The instant application partially describes the crystallization of a wild type mutants having C164 substituted with serine." (Office Action, page 3, lines 5-6; emphasis added)
- ". . . the specification fails to describe . . . a reproducible method to obtain the crystal" (Office Action, page 3, lines 11-13)
- "The crystallization condition at page 175, second paragraph, fails to identify the exact conditions, which the crystal can be grown." (Office Action, page, 3, last two lines)
- "Neither the composition of the protein solution nor the final composition, in which the crystal is grown, is taught in the specification." (Office Action page 4, lines 11-12).

5. Contrary to the various mischaracterizations set forth in Item 4 above, the specification fully describes crystallization conditions for chalcone synthase and specific mutant at page 175, second paragraph, i.e.,

> Crystallization. CHS crystals (wild-type and $C_{164}S$ mutant) were grown by vapor diffusion at 4° C in 2 µl drops containing a 1:1 mixture of 25 mg/ml protein and crystallization buffer (2.2-2.4 M ammonium sulfate and 0.1 M PIPES, pH 6.5) in the presence or absence of 5 mM DTT. Prior to freezing at 105° K, crystals were stabilized in 40% (v/v) PEG400, 0.1 M PIPES (pH 6.5), and 0.050-0.075 M ammonium sulfate. This cryoprotectant was used for heavy atom soaks. Likewise, all substrate and product analog complexes were obtained by soaking crystals in cryoprotectant containing 10-20 mM of the compound.

According to the method described in this passage, crystals of chalcone synthase (or mutant thereof) are grown by vapor diffusion. This technique is well known and routinely practiced in the field of crystallography. Drops (i.e., 2 µL in size) of a defined 1:1 mixture of (1) protein and (2) crystallization buffer are used for crystal growth at 4° C. The defined protein component prior to forming the 1:1 mixture is 25 mg/mL protein. The term "25 mg/ml protein" means exactly what it says, i.e., the protein is in water at a concentration of 25 mg/ml. The

defined crystallization buffer prior to formation of the 1:1 mixture is 2.2-2.4 M ammonium sulfate and 0.1 M PIPES, pH 6.5. In some experiments, DTT is present at a concentration of 5 mM.

6. Thus, each of the concerns raised in the Office Action (as summarized in Item 4 above) is fully addressed by the specification, which provides a complete and reproducible method for crystallization of chalcone synthase and mutants with exact conditions regarding composition of the crystallization liquor, concentrations of various components thereof, and temperature for such crystallization.

7. I further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

Date 9/28/06

Joseph P. Noel